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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/718,425	11/24/2000	Oren Becker	24460	1582
20529	7590	11/17/2006	EXAMINER	
NATH & ASSOCIATES 112 South West Street Alexandria, VA 22314			LIN, JERRY	
			ART UNIT	PAPER NUMBER

1631

DATE MAILED: 11/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/718,425

Applicant(s)

BECKER ET AL.

Examiner

Jerry Lin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) 18-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17, 22 and 23 is/are rejected.
- 7) ☒ Claim(s) 17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 May 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Upon further consideration of the prosecution history, the Notice of Abandonment sent September 6, 2006 has been withdrawn. Examination of the instant application will continue.

Status of the Claims

Claims 1-17, 22 and 23 are under examination.

Claims 18-21 are withdrawn as being drawn to an unelected invention.

Drawings

The drawings were received on May 25, 2004. These drawings are acceptable.

Claim Objections

2. Claim 17 is objected to because of the following informalities: there appears to be a typographical error where the phrase "Claim 17, line 1, delete 'or 16'." has been incorporated as part of claim 17. In addition, claim 17 is still dependent from claims 15 or 16, although it appears the Applicants only want claim 17 to be dependent from claim 15. Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-17, 22, and 23 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are drawn to a method of predicting an amino acid sequence by providing a coordinate set representing the backbone of a 3D structure, constructing a reduced virtual representation for the 3D structure, determining the amino acid positions along the 3D structure, constructing an initial amino acid sequence, randomly selecting one or more positions along the sequence and applying a Monte-Carlo simulation, and expanding the reduced representation.

In order to determine if a claimed invention has utility, the examiner must determine if the claimed invention has a specific, substantial, and credible utility or a well-established utility. A specific utility is defined as a utility that is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. A substantial utility is defined as a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A credible utility is determined from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles. Finally, a well-established utility is a specific, substantial, and credible utility which is well known, immediately apparent, or implied by

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the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The claimed invention lacks either specific or substantial utility. The instant claims are drawn to a method for the prediction of an amino acid sequence that is constructed via evaluation of solvent accessibility without any specific or substantial utility for the predicted protein or peptide. In part a) of claim 1, a 3D structure is set provided but without any specificity as to a connection to a utility for the structure. That is, there is no required substrate binding activity set forth. Alternatively, there is no recognition of a binding entity present as a claimed limitation nor set forth in the instant specification. Additionally, the solvent accessibility which is utilized in the claimed method to be compatible with the solvent accessibility at each position is not directed to a protein or peptide utility. Thus, a generic utility is apparently meant for the protein or peptide being predicted as to its amino acid sequence. A generic utility is not specific as required by 35 U.S.C. § 101. There is also a lack of a substantial utility as there is no substantial utility defined or even asserted for the predicted protein or peptide sequence as a result of performance of the methods as claimed either for enzyme activity or some type of binding or recognition activity such as present in proteins or peptides which act as receptors, for example, or possibly peptides which bind to receptors in order to produce some type of biological response for said binding. It is noted that claim 2 includes a native protein as an option for providing the 3D structure for part a) of claim 1. Nothing specific or substantial is therein set forth as to such a native protein, but rather a general or generic protein is set forth without further

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limitation regarding utility thereof thus additionally supporting this determination of a lack of specific or substantial utility. It may be postulated that the solvent accessibility is somehow related to protein or peptide utility in step c of instant claim 1. This, however, is not asserted as defining a utility for the practice of step c in the instant specification nor in the claims such that the solvent accessibility results in some type of protein or peptide utility. It is acknowledged that one aspect of a protein's or peptide's function includes solvent accessibility for binding activity, but that such solvent accessibility per se lacks specificity as to what binding then occurs for entities which have access via solvent accessibility. Is hydrogen bonding then utilized via such accessibility? Is there ionic bonding? Are other types of interaction/bonding then utilized for protein or peptide function or activity? At best solvent accessibility provides access but does not produce whatever interactions or bond availability thus results in a protein or peptide activity or function. Thus, the utility of predicting an amino acid sequence for a protein or peptide as instantly claimed lacks specificity or substantiality as to utility without some nexus to protein or peptide activity or binding reactions which will result in specific and substantial utility. It is noted that no well established utility has been asserted or is known for generic amino acid sequence prediction without some utility for the resultant protein or peptide. It is also noted that, in the absence of a well known utility, a utility must be substantiated which has the combination of specific, substantial, and credible utility. Since the instant invention as disclosed lacks either specific or substantial utility, the credibility is not required to be assessed. That being stated, it is acknowledged that

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protein or peptide design per se is deemed a credible utility for proteins or peptides with some function or activity which has both a specific and substantial use.

Response to Arguments

5. In response to this rejection, the Applicants stated that their application contains passages that disclose a utility for the invention as well as providing additional utilities for the Examiner to consider. However, the Examiner disagrees that the specification provides a utility that is substantial and specific or that provided additional utilities are substantial and specific.

The Applicants first cite page 15 of the specification. Page 15 of the specification provides that the amino acid sequence determined from the claimed invention may be produced through a host cell. The specification also states, "Once made, the novel amino acid sequence may be experimentally evaluated and tested for structure, function and stability as required." The specification clearly is stating that further experimentation is required to determine the utility of the claimed invention. However, utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. Thus this passage of the specification does not provide a substantial and specific utility are required by 35 U.S.C. §101.

The Applicants also provide additional utility such as Therapeutic proteins, biotechnology utilities, designing novel therapeutic proteins, building blocks for nanotechnology, and novel therapeutic peptides. Each of these utilities are based on

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the argument that new properties of the designed amino acid sequences may be found. However, in each case additional experimentation is required to discover these new properties. Since further research is required to identify or confirm a real world context of use, the additionally provided utilities are not substantial utilities and do not satisfy the requirements of 35 U.S.C. §101.

This rejection is maintained.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 22 and 23 are also rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a substantial or specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

This rejection is maintained for the reasons above.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-17, 22, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahiyat et al. (Protein Science, 1996, Vol. 5, pages 895-903), and further in view of Hurley et al. (JMB Vol. 224, 1992, pages 1143-1159).

The instant claims are drawn to a method of predicting an amino acid sequence by providing a coordinate set representing the backbone of a 3D structure, constructing a reduced virtual representation for the 3D structure, determining the amino acid positions along the 3D structure, constructing an initial amino acid sequence, randomly selecting one or more positions along the sequence and applying a Monte-Carlo simulation, and expanding the reduced representation.

Regarding claims 1-5, 9-17 and 22, Dahiyat et al. teaches protein design automation. Specifically they teach "We have conceived and implemented a cyclical protein design strategy that couples theory, computation, and experimental testing. The combinatorially large number of possible sequences and the incomplete understanding of the factors that control protein structure are the primary obstacles in protein design.

Our protein design automation algorithm objectively predicts protein sequences likely to achieve a desired fold. Using a rotamer description of the side chains, we implanted a fast discrete search algorithm base on the Dead End Elimination Theorem to rapidly find the globally optimal sequence in its optimal geometry from the vast number of possible solutions. Rotamer sequences were scored for steric complementarity using a van der Waals potential. A Monte Carlo search was then executed, starting at the optimal sequence in order to find other high-scoring sequences. As a test of the design methodology, a high scoring sequences were found for the buried hydrophobic residues of a homodimeric coiled coil base on GCN4-p1. The corresponding peptides were synthesized and characterized by DC spectroscopy and size exclusion chromatography. . . . A quantitative structure activity relation analysis was performed on the designed peptides, and a significant correlation was found with surface area burial. Incorporation of the buried surface area potential in the scoring of sequences greatly improved the correlation between predicted and measured stabilities and demonstrated experimental feedback in a complete design cycle.” (Abstract). Specifically, Dahiyat also teaches that the PDA side-chain selection algorithm requires as input a backbone structure defining the desired fold. Also taught is that “using a rotamer description of side chains, an optimal sequence for a backbone can be found by screening all possible sequences of rotamers, where each backbone position can be occupied by each amino acid and all its possible rotameric states.” (page 896). (This corresponds to steps (a) through (d) of claim 1.) Also taught is “following DEE optimization, a rank-ordered list of sequences is generated by a Monte Carlo search in the neighborhood of the DEE solution. . . random

position are changed to other rotamers, and the new energy is calculated. If the new sequence energy meets the Boltzmann criteria for acceptance, it is used as the starting point for another jump. . . after a predetermined number of jumps, the best scoring sequences are output as a rank-ordered list.” (Page 897). (This corresponds to step (e) of claim 1.) Also taught is that simpler structure measure, such as buried atoms, were used to resolve the structure of the amino acid. (page 899). (This corresponds to step (f) of claim 1.) Dahiyat et al. also teach using hydrophobic and hydrophilic positions to determine the structure (page 897). In regards to claims 8, 10, 11, since all positions are selected from the entire group of amino acids, these claims are fully anticipated.

However, Dahiyat et al. does not teach where at least one amino acid is represented by two or more spheres.

Regarding claim 1, Hurley et al. teach representing at least one amino acid by two or more spheres. (pages 1150-1153).

It would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate the representation taught by Hurley et al. with the method of Dahiyat et al. to gain the benefit of being able to determine the structural changes of a protein or peptide. The shape of the amino acid plays a large role in determining the overall structure of the protein. By representing an amino acid in the ball and stick representations presented by Hurley et al., one of ordinary skill in the art would be better able to determine the interactions among the amino acids. Given that the goal of Dahiyat et al. is to understand the factors influencing protein structure (abstract), one of

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ordinary skill in the art would be motivated to incorporate the representations by Hurley et al. with Dahiyat et al. to gain the benefit of determining structural changes.

Regarding claims 6-8, Hurley et al. teaches design and structural analysis of alternative hydrophobic core packing arrangements in bacteriophage T4 lysozyme. Particularly, they teach, "in order to calculate stability changes in aqueous solution, the changes in free energies of transfer of the folded and unfolded states between water and vacuum must be obtained." (Page 1146).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teaching of Dahiyat et al. and those of Hurley et al. As Hurley taught, it would have been obvious to determine the structure of an amino acid in water because it would have allowed for the calculation of stability change. Also, water would have been a common solvent for the amino acid structures to be found in nature, and therefore would have been obvious to use as it would have allowed for the closest approximation to nature. Furthermore, water would have been obvious solvent due to its neutral pH, low cost, and easy availability.

Response to Arguments

9. The Applicants have responded to this rejection by stating that neither Dahiyat et al. or Hurley et al. teach the amended limitation of "wherein in said reduced representation, each amino acid is represented by one or more spheres, and at least one amino acid is represented by two or more spheres." The Examiner disagrees. As

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explained above, Hurley et al. teach representing at least one amino acid by two or more spheres (ball and stick representation). (pages 1150-1153). Thus the combination of Dahiyat et al. and Hurley et al. teaches all of the limitations of the instant claims.

This rejection is necessitated by amendment.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 10:00am-6:30pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Representatives are available to answer your questions daily from 6 am to midnight (EST). When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

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also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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MICHAEL BORIN, PH.D
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Michael Borin', written in a cursive style.

JL